function of the chip design. In certain embodiments of the invention the attachment locations form a grid-like pattern as in conventional oligonucleotide or cDNA microarrays, and the chip configuration is optimized such that a single bead is attached at each occupied attachment location. The distribution is random in the sense that a particular bead may attach to any attachment location. In certain embodiments of the invention the density of attachment locations is greater than 10,000 per mm^2, making the arrays suitable for high throughput applications and offering the potential for an "array of arrays" format on a single chip.

[0053] The sample can be contacted with the beads prior to their dispersal on the chip or after dispersal has occurred. For example, when the assay involves nucleic acid hybridization, beads with attached probes can be mixed with sample prior to dispersal, or hybridization can be performed after the beads are attached to the chip. The identity of the bead, and thus of the probe associated with that bead, can be encoded using any of a variety of approaches as described below. Interaction (e.g., binding) between the probe and a target can be detected and the identity of the bead determined by appropriate decoding. Alternately, the identity of the probe can be determined directly (e.g., by microsequencing in the case of a DNA probe).

[0054] **FIG. 1** presents a conceptual outline of a typical assay (e.g., a hybridization-based assay) that may be performed according to the invention. **FIG. 1**(A) represents three populations **12**, **13**, and **14**, of magnetic beads. Typically the beads in each population will have been labeled, e.g., with a fluorescent dye or hybridization tag, so that beads from a given population may later be distinguished from beads of a different population. However, this need not be the case. The beads will typically be in a fluid medium. Different probes **22**(*b*), **23**(*b*), and **24**(*b*) are attached to beads **22**(*a*), **23**(*a*), and **24**(*a*) forming bead-probe units **22**, **23**, and **24**. Each probe is able to detect a particular target. For example, each probe may be a nucleic acid that is complementary to a particular target nucleic acid.

[0055] As shown in **FIG. 1**(B), beads from each of the populations are combined to form a mixture **15**, to which a sample containing one or more target molecules **31** is added. Typically the target is labeled in some fashion so that it is detectable. The sample could also be added to the individual bead populations prior to mixing. The relative number of beads from different populations may be varied, e.g., depending upon the expected abundance of target, the sensitivity desired, etc. In general, any number of beads from the multiple populations can be used, depending upon the redundancy desired. The sample may contain a single type of target molecule or multiple different target molecules, and the abundance of the target molecule(s) may vary. The mixture is incubated for a period of time to allow interaction between probe(s) and target(s). For example, in a hybridization-based assay the mixture would be incubated to allow hybridization between complementary probes and targets.

[0056] Following the incubation period the beads are introduced to the magnetic chip **28** by any convenient means, e.g., using a pipette or via a channel. As shown in **FIG. 1**(C), the magnetic chip includes magnetic regions **26** referred to as magnetic islands, positioned in a regular pattern on a substrate **25**. The beads are immobilized by the localized magnetic field that exists between adjacent magnetic domains. Following a brief period (e.g., seconds to minutes) during which bead trapping takes place, excess bead solution containing unbound beads is removed. While the possible sites at which beads may be trapped are arranged in a regular pattern, the final arrangement of beads is random, as described further below. **FIG. 2** shows a conceptual image of a magnetic chip containing diamond-shaped magnetic regions with arrayed beads. After formation of the array and removal of excess beads, the beads, probes, and/or targets may be detected according to any appropriate detection means, after which the beads can be removed, e.g., using a fast fluid flow. The chip may then be reused.

[0057] In general, the bead or its attached probe will have been labeled with some detectable moiety, and the target will have been labeled with a different detectable moiety. The labeling of the target allows detection of the interaction between probe and target, while the labeling of the bead or probe allows identification of the probe, which may further identify or indicate the presence of the particular target with which that probe interacts. Interactions may include binding (e.g., in the case of a hybridization-based assay) but may also include enzymatic reactions, etc. Interaction may result in quenching of a detectable marker, occurrence of an enzymatic reaction that may be detected, etc. As will be evident to one of ordinary skill in the art, numerous variations on the preceding scheme are possible, some of which are described in further detail below.

[0058] According to certain embodiments of the invention the chip is produced using variations of conventional semiconductor fabrication methods. Like other semiconductor fabrication methods, this is a readily scalable technology. The invention presents a number of other advantages over existing technologies for forming either positionally encoded or randomly ordered arrays. Among these are multiple reuse via a simple wash and/or demagnetization, simplicity and flexibility of chip design and fabrication, compatibility with on-chip electronics such as photodetection, and direct compatibility with bead-based nucleic acid/protein protocols. These include essentially any of the numerous assays for which substrate-bound oligonucleotide or cDNA arrays are currently employed.

[0059] In general, the use of bead-based approaches offers significant advantages over arrangements in which probe is bound to substrate. Once a substrate-bound array is prepared, changing or adding probes requires fabrication of a new array. In contrast, with bead-based approaches a new probe may be substituted or added by simply preparing a population of beads bearing that probe. The selection of probes is entirely flexible and can occur at the time of teh assay rather. The degree of redundancy can be varied by varying the number of beads that bear any particular probe and/or by varying the ratio of beads bearing different probes. Thus the assay can be conveniently tailored as desired by the practitioner, depending on the particular application, instead of being constrained by a selection of probes that was made by a chip manufacturer.

[0060] The fact that assays involving interactions between molecules (e.g., hybridization between probe and target, enzymatic reactions, etc.) can be performed on the surface of a mobile bead in a tube rather than on an immobile surface provides further advantages. Rather than a situation in which